Preliminary Descriptive Statistics of the Taiwanese Registry of Epilepsy and Pregnancy for the First 2 Years

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SUMMARY

Objective: To present the descriptive statistics of the Taiwanese Registry of Epilepsy and Pregnancy (TREP) for the first 2 years.

Materials and Methods: The pregnancies were recruited from May 2004 to January 2006 with a data format compatible with the International Registry of Antiepileptic Drugs and Pregnancy (EURAP) by referral. The data were collected from either face-to-face interview, telephone interview, or chart review by a research nurse. Five questionnaires (A–E) were required for each pregnancy. The preliminary data for the first 2 years are presented with general descriptive statistics.

Results: Until January 2006, 43 pregnancies have been registered. Questionnaire A was completed in 43 cases, questionnaire B completed in 40 cases, questionnaire C completed in 34 cases, questionnaire D completed in 27 cases, and questionnaire E in eight cases. Among the 39 pregnancies known to take antiepileptic drugs (AEDs) during pregnancy, 28 pregnancies took one AED, nine pregnancies took two AEDs, and two pregnancies took three AEDs. The most commonly used drug was carbamazepine (19/39, 48.72%). Among the 27 pregnancies, who had delivered, the cesarean section rate was 44.44% (12/27), the premature birth rate was 7.41% (2/27), and the fetal malformation rate was 3.7% (1/27).

Conclusion: The preliminary data concluded the efforts of TREP for the first 2 years. Although it is still premature to project a trend out of current data, the registry is expected to provide critical information to local prenatal counseling and contribute further to the international EURAP database. [*Taiwanese J Obstet Gynecol* 2007;46(1):47–49]

Key Words: antiepileptic drugs, epilepsy, EURAP, pregnancy, pregnancy registry, TREP

Introduction

The safety of antiepileptic drug (AED) use in pregnancy has been an unsolved puzzle for generations. Given the fact that women with epilepsy compromise only around 1% of the population, tend to have a decreased fertility rate, and are generally socially and economically disadvantaged, conclusions derived from individual clinical researches are generally limited by their statistic power due to the small sample size. To solve this problem, pregnancy registries for women with epilepsy were founded to pool individual data series together to gain a whole view of the issue [1–4].

The Taiwanese Registry of Epilepsy and Pregnancy (TREP) was officially launched in 2004 by Dr Chi-Wan Lai with the cooperation of the Taiwan Epilepsy Society

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and the Taiwan Society of Perinatology and joined the International Registry of Antiepileptic Drugs and Pregnancy (EURAP), an international AEDs and pregnancy registry originated in Europe, in the same year. The data center and relevant services are maintained and staffed at the Pregnancy Assessment Center in the Mackay Memorial Hospital, Taipei, Taiwan. The descriptive statistics of the first 2 years and relevant discussion are presented in this article.

Materials and Methods

The patients were recruited from May 2004 to January 2006 and the data were stored in a central database of the TREP managed by the Taiwan Epilepsy Society and the Taiwan Society of Perinatology. The data format was based on the five questionnaires (A–E) of the EURAP and was also customized for our local needs. Questionnaire A was to be completed as early as possible if pregnancy was confirmed. Questionnaire B was to be completed at 14–24 weeks, questionnaire C at 24–28 weeks, questionnaire D at birth, and questionnaire E at 1 year of age. A telephone help line was offered to the general public for general enquiry, health education, and data collection. Women with epilepsy who became pregnant were eligible to register. The data were collected by a research nurse in the Pregnancy Assessment Center of the Mackay Memorial Hospital, Taipei, Taiwan with either face-to-face interview, telephone interview, or chart review. The patients were referred by their doctors or they might also be self-referred with the telephone help line. All patients were asked to sign a consent form and the patients meeting the data collection criteria of EURAP were pooled to the EURAP database with the provided software from the EURAP. The patients in the TREP database were reviewed with general descriptive statistics.

Results

Until January 2006, there were 43 singleton pregnancies, totally 41 women, registered in the central database. There were no multiple pregnancies in our series. Among the registered pregnancies, 14 were entered in 2004 and 29 in 2005. Questionnaire A was completed in 43 pregnancies, questionnaire B completed in 40 pregnancies, questionnaire C completed in 34 pregnancies, questionnaire D completed in 27 pregnancies, and questionnaire E completed in eight pregnancies. Among the 43 pregnancies, 36 (36/43, 83.72%) pregnancies were referred by their doctors, and seven (7/43, 16.28%) pregnancies were self-referred.

The use of AED was not specified in three pregnancies (3/43, 6.98%) and the use of AED has been stopped before pregnancy in one pregnancy (1/43, 2.33%). Among the 39 pregnancies with the use of AED specified in the database, there were 28 pregnancies taking one AED (28/39, 71.79%), nine pregnancies taking two AEDs (9/39, 23.08%), and two pregnancies taking three AEDs (2/39, 5.13%).

The most commonly used drugs were carbamazepine (19/39, 48.72%), phenytoin (8/39, 20.51%), lamotrigine (7/39, 17.95%), valproate sodium (7/39, 17.95%), topiramate (5/39, 12.82%), and phenobarbital (3/39, 7.69%).

Among the 27 pregnancies which had delivered, there were 12 cesarean sections (12/27, 44.44%) and 15 vaginal deliveries (15/27, 55.56%). The premature birth rate was 7.41% (2/27), with one at 34 and the other at 35 completed weeks. Fetal distress leading to cesarean section was reported in three pregnancies (3/27, 11.11%) and there was one breech (1/27, 3.7%). One woman had an epilepsy attack in the postoperative room after the cesarean section (1/27, 3.7%). No other significant pregnancy complications were reported. In addition, fetal malformations were found in one infant after birth (1/27, 3.70%) in one pregnancy taking phenytoin and valproic acid. The infant was small for the gestational age and the malformations included preaxial polydactyly in the left hand, low-positioned thumb in the right hand, postaxial polysyndactyly in the right foot, rocker-bottom feet, arachnodactyly, craniosynostosis of the metopic and coronal sutures, microcephaly, and trigonocephaly.

Among the 43 registered singleton pregnancies, there were 35 primigravida (35/43, 81.40%) and there were 11 children delivered in the previous pregnancies. No malformation was reported in the 11 children by the women. There were three pregnancies resulting in intrauterine fetal death at 12 weeks in the database. Among them, two pregnancies were of the same women taking carbamezepine; however, the use of AED was not specified in the other pregnancy.

The average maternal age on the expected date of delivery was 28.50 years, and the standard deviation was 3.87 years. Among the delivered term pregnancies, the average birth weight was 2,925.07 g, and the standard deviation was 439 g.

Discussion

Teratogenicity is a major concern of the pregnant women with epilepsy who choose to reproduce. In addition, it is generally believed that pregnant women with

epilepsy tend to have a higher incidence of pregnancy complications; however, Richmond et al reported that although the rates of nonproteinuric hypertension, induction of labor, and fetal cardiovascular malformations were increased in pregnant women with epilepsy, the rates of other antenatal, intrapartum, and neonatal complications and congenital malformations were similar to the women without epilepsy [5]. Richmond et al also concluded that as long as appropriate care is taken to the pregnant women with epilepsy, they are not at an increased risk of having obstetric complications. Endo et al also reported that for pregnant women with and without epilepsy, no significant difference was found in complications during pregnancy, types of delivery, or complications at delivery, excluding the frequency of abnormal rotation in the birth canal [6]. Although our result is still preliminary, the rates of major malformation and pregnancy complications seem to be not increased.

There was one case of malformation in our 27 delivered singleton pregnancies. The woman took phenytoin and valproate sodium before pregnancy and through pregnancy, exposing her to the risks of fetal hydantoin syndrome and fetal valproate syndrome [7]. She was prescribed to take folic acid in pregnancy; however, she was low in socioeconomic status and was not quite compliant with the prenatal care. As the use of valproate during pregnancy is associated with an increased risk of major congenital malformations and developmental delay [8], it was suggested that pregnancies in women taking valproate should be planned to minimize the risk of malformation [9]. In contrast, the use of phenytoin in pregnancy is not associated with an increased risk of malformation, either in monotherapy or in polytherapy without valproate. However, the postnatal findings suggest that both phenytoin and valproate might have contributed to the phenotype of the newborn.

It was reported that carbamazepine as monotherapy was associated with the lowest risk of major congenital malformation [10]. Among the 39 pregnancies with the use of AED specified in our series, 13 pregnancies (13/39, 33.33%) used carbamazepine as monotherapy.

Olafsson et al reported a twofold increase of the cesarean section rate in pregnant women with epilepsy in Iceland given the fact that the incidence of adverse events during pregnancy for pregnant women with epilepsy was not different from the general population [11]. Our series also shows a high cesarean section rate at 44.44%, and this suggests the decision to have a cesarean section might not be limited to obstetric indications and this warrants further analysis in the future.

In conclusion, our article presents the preliminary descriptive statistics of the TREP, and it portrays a general level of care and serves as an auditing tool of clinical practice for pregnant women with epilepsy in Taiwan. The registry will be carried on as a joint project of the Taiwan Epilepsy Society and the Taiwan Society of Perinatology.

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